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THE AMERICAN
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VOL. 105 OCTOBER, 1933 NO. 10

EDITORIAL

"SCIENCE DRAWS VEIL OFF CREATION"

WHAT we presently know regarding the origin of life is that we know nothing. And that is usually a fine premise upon which both to speculate and to work.

Recently the daily press captioned an article dealing with the researches of Bainbridge (Bartol Fellow of the Franklin Institute in Philadelphia), captioned it with the big black-lettered phrase, *"Science Draws Veil Off Creation."*

To the credit of the daily press it should be stated that scientific news are now reported in the columns of our leading papers more accurately and less sensationally than ever before—and this in spite of the fact that there are left still enough pseudo-scientists of subtle and plausible technique, who, for a paltry bit of publicity, will arrantly and purposely mislead a perfectly well-meaning and ethical reporter of news.

This latter statement has, of course, no bearing whatever on the Bainbridge report, which, outside of its startling caption, "Science Draws Veil Off Creation," is a clear and probably a correct description of an unusual discovery in the field of physics.

For the first time, in practice, *man seems to have transmuted energy into matter.* Certainly, theorists have for years maintained that this could be done. But it remained for Dr. Kenneth Bainbridge to do it and to do it in a way allegedly capable of proof and of repetition. He showed that when the metal lithium is bombarded with alpha particles traveling about 10,000 miles a second, the bombardment yields the element boron plus one neutron. The neutron is a recently found and christened particle having no electrical charge. The alpha particles used were helium nuclei thrown off by the chemical element, polonium.

This boro-neutron product of the bombardment, when weighed, proved to be heavier than the sum of all materials which made it. Specifically, an original mass of 11.01416 on the atomic scale, had become 11.0202. The gain in weight was .00604.

There was nothing to account for this increase in weight except that the speed of the alpha particles had been converted into solid matter.

"Can this be a case," Dr. Bainbridge asked when he made the report, "in which the energy of motion of the alpha particle is transformed into mass,—a creation of matter from energy?"

This seems to make it necessary for us to revamp our ideas of the old laws of matter's indestructibility and the conservation of energy. But Dr. Bainbridge is hesitant. "Can it be so?" he queries!!

Our morning paper states, and without equivocation, "It is so!!" —*"Science Draws Veil Off Creation."*

But we hazard the guess that it will be many a merry day of search and research before that caption stands unchallenged.

A thousand ages may be lost in Time's abyss, with man still groping fo Life's secret—but there will always be ample jusification for pressing the search and a still more ample right to hope for its eventually inevitable solution.

What to do with it—if ever the problem does yield its answer—that is the question.

Possibly, by that time, humanity will have achieved to those godly eminences which confer a vision, clearer and more understanding, than that which is ours, in the valleys, today.

IVOR GRIFFITH.

Vitamin A and Carotene Isomers

α-and-β-carotene have been separated by preferential chromatographic adsorption on calcium hydroxide or monoxide. The α-form was obtained in a pure state, melting at 187 degrees C. (corr). The absorption spectra in antimony trichloride solution of the separated forms showed that the band at 590 μ belongs to the β-form, and that at 542 μ to the α-form. A vitamin A preparation, after separation by adsorption on calcium hydroxide gave fractions yielding single adsorption bands.—Karrer, Walker, Schöpp and Morph (*Nature,* (1933), 132, 26).

FROM ORIGINAL, VERY ORIGINAL, SOURCES

ONE of the routine duties of an editor is to scan the current literature in his special field and wield his scissors where he wills. Nor is this *routine* duty altogether a drab and dreary job. No indeed! For the oddities of editors, the cussedness of compositors and the tantrums of typesetters frequently fashion a fun and a farce that liven and leaven the work.

Scientific literature is obviously more meticulously compiled than the regular run of fiction and fact, but even into it, carelessness too commonly creeps. Medical, chemical and pharmaceutical journalism is not without its absurdities. And this, unfortunately, is particularly true of the polyglot pharmaceutical literature, where shop notices and professional items are so often hodgepodged together.

Witness the following parade of freaks and monstrosities culled from several such sources. Note the queer Englishing in many spots, the gross inaccuracies, the vapid giving vent to words, and the frequent lack of sense and style and system.

Origins are not announced and each item is printed without a change. Let those whose works these are, recognize but not acknowledge them.

We, too, live in a transparent house, and know its inviting glassicity. Let those who may, or must, cast stones wherever, whenever they will,—we shall use them for building.

> Question—Name the tinctures which are quite strong in alcoholic content and suitable as vehicles or flavoring agents.
>
> Answer—The following are such official tinctures: Tincture Aromatica, Tincture Cinnamomi, Tincture Zingiberis, Tincture of Sweet Orange, Tincture of Bitter Orange, Tincture of Lemon Peel, Tincture of Cardamom, Compound Tincture of Cardamom, Compound Tincture of Lavender, etc.

Latin is a *dead* language—but here decomposition has set in.

> Historical Medicine. By Edward Podolsky, M. D. This interesting article tells of the use of bees in medicine and it is timely.

Where bees made history!

> Bollettino Chimico-Farmaceutico, Milano, July 30, 1932. (A New Source of Borax.)—At 6:30 a. m., June 9, 1932, a terrific explosion took place at the Serrazzano plant, (Pisa), about 10 kilometers away from the Lardello's Borax Zone. The hole caused by the explosion is 184.40 meters deep and has a diameter of 30 cms. The vapor liberated was calculated at 150,000 Horse-Vapors per hour.

Page the twenty-mule team!

"In answer to the question as to how Man first learned of the fact that herbs of one sort or another possessed medicinal virtues, it may be said that his first knowledge of this kind was no doubt obtained by watching the animal in times of bodily distress. It is a well-known fact that animals seek certain herbs when in need of a purgative or an emetic. Today one can witness a certain fondness on the part of cats for Catmint as well as for Valerian."

Exactly, as man learned the joys of tobacco by watching a goat smoke a pipe.

Question—In making Barbital Sodium Tablets, I notice that the finished product usually is of a pink shade. What is the reason for this and can I dispense?

Answer—No, do not dispense. The trouble probably lies in the fact that the mortar is not clean. Due to an alkaline-like MgO of which some parts may have stuck to the mortar, the preparation would turn to a pinkish shade. All precautions should be taken that the mortar is cleaned before starting to work with the Barbital. This can easily be done by washing with HCl.

That must be the answer! it is so labeled.

For Sale—Drug store in Missouri City, Mo. The town is wet, the doctor is wet, and the drug store will be a gold mine for a wet druggist. Rent $15.00 and living quarters in brick store building. Will sell for cash only. S. F. Fleming, Missouri City, Mo.

O tempora! O mores!!

"The town is wet, the doctor is wet"—and when they find the wet druggist—they will be *"all wet."* And this from a reputable pharmaceutical journal!!

"After the visitors turn here, they are confronted with a spectacular entertainment of various bits of 'Pharmacy' science. Before them is a replica of the famous 'Rosetta Stone' unearthed by one of Napoleon's lieutenants during the Napoleonic wars, yet remaining valueless until the latter part of the twentieth century when that part of the stone that had to do with drugs was decipherable, and from which the prehistoric knowledge of Pharmacy was unfolded to the world."

O yes?

National Rat Week—Hints for the Chemist.—National rat week has been fixed this year to begin on Monday, November 7, and the Ministry of Agriculture has invited the co-operation of all local authorities to ensure a concerted action for the destruction of rats and mice.

What do they mean by "Hints for the chemist"?!!!

An Extraordinary Patent, U. S. Patent No. 1,780,981, issued November 11, 1930, to Mary B. Parrish, of Philadelphia, Pa., makes the following unusual claims:

A process of amplifying anilin dye colors comprising predigesting an anilin dye in the presence of pancreatin, ox gall, sodium chloride, citric acid, acetic acid and acetone; thereafter boiling the resulting mass with a mixture of soap and tinctures of vegetable fixatives consisting of camomile flowers, hyssop, ground cedar wood, and myrrh and permitting the mass to cool to blood heat; then redigesting the mass by adding pancreatin, gelatin, acetone, sodium chloride, ox gall and acetic acid at blood heat and permitting the resulting product to ferment in a warm room for approximately two weeks; and thereafter mixing the resulting product with dextrin and baking the mass at bread baking temperature until the product is of a crisp consistency.

The specifications neglect to state whether it shall be Roman or German chamomile, and particularly that this process is only successful if carried out on a Tuesday.

"Social and business conditions here are not as precarious as one might expect, at this time, in an over-populated country such as Italy is and with resources limited."

"Regarding pharmacists and pharmacies, things look to me unquestionably better on this side, at least morally and hourly."

Again proving that Pharmacy does need as Mussolinioid Dictator.

"Dr. Quicksall declared that sodium nitrite usually is dispensed in powder or tablet form, and said he never saw it in stick form. He said there is a great difference between sodium nitrate and sodium nitrite in chemical composition, the former being known commonly as saltpeter and the latter being a complicated organic compound."

This comes under the general caption of *"expert testimony."*

And so we might go on with merry repetition. But sufficient has been submitted to prove that pharmaceutical "literature" does need a little purging.

IVOR GRIFFITH.

"If the political aspirations of the nations should grow sane, and the artificial economic problems of the world be solved, the combined and assured gifts of health, plenty and leisure may prove to be the final justification of applied science. In a community, advantaged by these, each individual will be free to develop his own innate powers, and, becoming more of an individual, will be less moved by those herd instincts which are always the major danger to the world. I believe that for those who cultivate it in a right and humble spirit, science is one of the humanities; no less."

SIR F. G. HOPKINS.

ORIGINAL ARTICLES

THE BACTERICIDAL EFFICIENCY OF MENTHOL AND CAMPHOR

By Louis Gershenfeld, P. D., B. Sc., Ph. M.,[1]

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MENTHOL and camphor have been tested for their bactericidal action, preservative effects and antifermentative powers in aqueous and alcoholic solutions and as vapors. The purpose of this paper is to set forth the results obtained from tests of menthol and camphor solutions in solvents of liquid petrolatum; in water; and in a solvent composed of alcohol, glycerin, water and soap.

Rippetoe and Wise (1) prepared saturated aqueous solutions of different oils and tested their preservative action against molds. They found that menthol acted as a preservative under these conditions. Harvey (2) used aqueous solutions of the essential oils to test the ability of these oils to stop the fermenting powers of yeast. Figures are given which represent the per cent. efficiency based on the antihydrolyzing power of the oil in a yeast sugar solution at the end of eight hours. Camphor had a value of twenty and peppermint a value of twenty-eight. Morel and Rochaix (3) tested both the vapor and the solution of various oils and found menthol to be more efficient in solution than in vapor.

Rideal, Rideal and Sciver (4) studied the relation between the lowering of surface tension caused by essential oils and their germicidal powers by measuring the "drop numbers" of the essential oil dissolved in pure paraffin. It follows from the theory that the greater the drop number (the number of drops formed as the paraffin solution of oil falls a certain distance) the greater the capillary effect and the greater the lowering of the surface tension. Several graphs were given which showed that oils with the highest "drop numbers" are also the best germicides. The germicidal tests were made according to the Rideal Walker technique of the phenol coefficient test,

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with B. typhosus as the test organism. Japanese mint (dementholated) tested in a 20 per cent. soap emulsion had a phenol coefficient of 0.7. White camphor had a phenol coefficient of 0.4. The same authors (4) also listed phenol coefficients as determined, according to the Rideal Walker method, by Penfold and Grant. Menthol is listed as having a phenol coefficient of nineteen, synthetic menthol as twenty, isomenthol as twenty and camphor as six. Rideal, Sciver and Richardson (5) using the Rideal Walker method for phenol coefficients give that of synthetic menthol as 0.9 and natural menthol as 0.4. Wokes (6) tested the antiseptic value of menthol isomers against B. coli and Staphylococcus aureus. The isomers were arranged in the following descending order of germicidal activity against B. coli: d. l.-neo-menthol, d.-menthol, d. l.-(racemic)-menthol, d. l.-iso-menthol, and l. menthol. Their germicidal activity against Staphylococcus aureus arranged in the following descending order was: d.-menthol, d. l.-iso-menthol, d. l.-neo-menthol, d. l.-(racemic)-menthol, and l.-menthol. He also found that an increase in the experimental temperature of about 10 degrees C. produced a small increase in the activity of phenol, but a considerably larger increase in the activity of the menthols.

Menthol is a saturated secondary alcohol ($C_{10}H_{19}OH$). Camphor is a dextrorotatory ketone ($C_9H_{16}CO$). Sollman (7) states that alcoholic solutions of menthol are antiseptic. Camphor is described by him as a mild irritant and feebly antiseptic, the isomers being about equivalent. It is employed as an intestinal antiseptic, with doubtful usefulness as a stimulant mouth wash and gargle in saturated solutions, and as a preservative for hypodermic solutions. Dixon (8) states that externally camphor has a mild antiseptic action while menthol is more strongly antiseptic than camphor. It is excreted in the urine as menthoglycuronic acid, which it renders aseptic. Butler (9) describes menthol as an antiseptic, antipruritic, analgesic and anesthetic, as well as a germicide. It is used extensively in headaches, being rubbed on the forehead. Owing to its analgesic properties, it is used in the form of an ointment in various strengths for painful hemorrhoids, burns, boils and superficial inflammations. It is an ingredient of many sprays and lotions for the treatment of diseases of the ear, nose and throat. As an antipruritic menthol is said by him to be a valuable remedy to relieve the itching of eczema, pruritus and urticaria. In small doses menthol has been given to

allay nausea and vomiting and to relieve the pains of gastralgia. Camphor, according to Butler (9), is used for its antispasmodic action on the nervous system. It has an anesthetic effect upon the unbroken skin, but in a concentrated state it is very irritating to mucous membranes. It is a powerful parasiticide. When used as an antispasmodic, it is a stimulant to the cerebrum, producing a gentle exhilarating effect upon the brain, and a feeling of warmth in the system. It exerts a calmative influence upon certain nerve centers, allaying nervous excitement and muscular spasm. Excessive doses may cause delirium, and in the monobromated form, camphor causes muscular weakness, passing into paralysis, followed by stupor and collapse. It may cause mental confusion, headache, vertigo, dryness of the mouth and thirst, flushing of the face, clammy perspiration, disturbances of digestion and strangury. It is claimed that camphor may also possess mild aphrodisiac properties. Camphor, he states, is used locally, its anesthetic and antipruritic properties rendering it of great value in the treatment of skin diseases.

Merck's Index (10) states that menthol exerts analgesic, anesthetic and antiseptic action. It is used internally in vomiting, in gastric pain, in the dyspepsia of chlorosis, in phthisis and neurasthenia and as a gastro-intestinal antiseptic. Externally it is used in the treatment of headache, toothache, neuralgia, insect bites and pruritis. There are many preparations of menthol in the National Formulary. Camphor is described in Merck's Index (10) as a stimulant, diaphoretic, counter-irritant, sedative, expectorant, antiseptic, analgesic antipruritic and carminative. It is used internally in conditions of collapse, typhoid, cholera, dysentery, cardiac weakness and circulatory disturbances, rheumatism, gout, chordee, spasmodic cough, asthma, pneumonia, delirium tremens, nervous diarrhea, flatulence, colic and headache. It is used subcutaneously in olive oil solutions in phthisis and pneumococcic pneumonia. It is used externally in neuralgia, toothache, indolent ulcer, parasitic skin diseases and coryza. Merck's Index (10) states further that there are many preparations in the National Formulary. The United States Dispensatory (11) states that menthol in large doses is a narcotic, paralyzing eventually both the sensory and motor systems. It cannot be regarded as highly toxic. When locally applied it stimulates the nerves for the perception of cold, but depresses those for pain. It is actively antibacterial. Benefits from its external use in headache and other forms of

neuralgia are due to its counter-irritant rather than its anesthetic action.

Halsey (12) in his translation of Meyer and Gottlieb's Pharmacology states that when menthol is given in doses of 6.0 gm. per diem enough is secreted to sterilize the bile. Solis-Cohen and Githens (13) say that menthol is used externally as an unguent or liniment for its anesthetic and antibacterial effects. Regarding its antipathogenic action they state that although the power of even saturated solutions to destroy bacteria is not very great, 0.1 per cent. will prevent the growth of both pathogenic and putrefactive organisms. A saturated solution in oil blown into the nose seems to inhibit the activity of the pus cocci usually found in acute rhinitis. Cushny (14) states that camphor is possessed of some antiseptic action although it is much weaker than some of the members of the carbolic acid group and also than many of the volatile oils. It is used as an intestinal disinfectant and is excreted in the urine as uramidoglycuronic acid and also in combination with glycuronic acid.

Fox (15) performed experiments in which he sprayed rabbits' nasal mucosa once daily for nine months with solutions of menthol, camphor and eucalyptol in petrolatum. He used liquid petrolatum solutions of 1 per cent. menthol, 5 per cent. menthol, 5 per cent. camphor, 5 per cent. eucalyptol and liquid petrolatum as a control. He reports that animals tested with 5 per cent. menthol fared the worst; with 1 per cent. menthol better; with eucalyptol and camphor, about the same, but better than those in the 1 per cent. menthol group. The animals sprayed with liquid petrolatum alone fared the best.

Various thoughts have been propounded as to the efficacy of menthol and camphor sprays. Are the benefits derived due to partial anesthesia; are they merely of a physiologcial character; or are they due to the protective action obtained from a solution of these substances? Is it possible that if there are benefits, they may be merely due to the detachment of adherent mucus by the fresh secretion which follows the slight counter-irritation produced when using these products or are they employed solely as a placebo? There are, however, some (as presented here) who have claimed from time to time bactericidal virtues for these substances and it is to determine this latter factor that the following experiments were conducted.

TESTS

Menthol and Camphor in Liquid Petrolatum

Solutions of 1 per cent. menthol, 1 per cent. camphor and a mixture of 1 per cent. menthol and 1 per cent. camphor were prepared using liquid petrolatum as the solvent. Tests extending over a period of two hours were performed on these liquid petrolatum solutions. Staphylococcus aureus (209) was employed at a temperature of 37 degrees C. and Bacillus typhosus (Eberthella typhi-Hopkins' strain) at a temperature of 20 degrees C. Five cc. of each solution and 0.1 cc. of the test organism were mixed and transplants of a (standard 4 mm.) loopful of this mixture were made into tubes containing 10 cc. of sterile bouillon every ten minutes for two hours. The tubes were incubated at 37 degrees C. for forty-eight hours and readings were made. The undiluted solutions and the plain liquid petrolatum (as a control) were tested. In all cases growth was found in every tube.

Since the liquid petrolatum solvent (being immiscible with water) would not mix with the bouillon cultures of the test organisms, it was impossible to perform the phenol coefficient test and a modification of this test was devised. Five-tenths of a cc. of a twenty-four-hour old culture of Staphylococcus aureus (amount used in phenol coefficient tests) was placed in a centrifuge tube and centrifuged at a high rate of speed for five minutes. The supernatant fluid was poured off, five cc. of the petrolatum solution to be tested were added to this sediment of organisms, the latter stirred up with a sterile platinum wire, and the test carried out according to the Reddish method. The undiluted solutions of camphor and menthol in liquid petrolatum (strengths as previously mentioned) and also the solvent, liquid petrolatum, were used. Growth was observed in all subculture tubes.

The wet and dry filter paper methods as described by the United States Department of Agriculture Circular No. 198 (16) were performed on the undiluted solutions of menthol and camphor in liquid petrolatum and in no instance was the test organism killed. Pieces of No. 2 Whatman filter paper, about 0.5 cm. square, were sterilized in a Petri dish at a temperature below 170 degrees C. to prevent charring. These sterile papers were then impregnated with Staphylococcus aureus by immersion in a twenty-four-hour-old broth culture of the organism. A wet inoculated square was then placed in five cc.

of each petrolatum solution in such a way as to be completely covered and in intimate contact. At the end of five, ten and fifteen minutes, the wet papers were removed with a sterilized stiff platinum wire (bent at an angle) and placed in ten cc. sterile bouillon. After as much of the disinfectant as possible was removed, the squares were retransferred to a fresh tube containing ten cc. of sterile broth, the tubes were incubated at 37 degrees C. for forty-eight hours and readings were made. The dry filter paper method is similar to the wet filter paper test. Squares of filter paper are used which have been impregnated as described under the test above, except that the squares are dried for two days before use in a sterile Petri dish in an incubator at 37 degrees C.

In no instance was antibacterial action displayed by these petrolatum solutions of menthol and camphor in the tests herein outlined. Many of these tests parallel practical conditions. Therefore, any beneficial therapeutic effects obtained from the menthol—camphor solutions in liquid petrolatum, in the strengths commonly employed, are not due to any bactericidal action.

Tests With Saturated Aqueous Solutions of Menthol and Camphor

Saturated aqueous solutions of menthol and camphor were prepared and tested for their bactericidal efficiency. Five cc. of each solution were mixed with 0.5 cc. of a twenty-four-hour-old culture of Staphylococcus aureus at 37 degrees C. and transplants (a standard loopful) were made into tubes containing ten cc. of bouillon after five, ten, fifteen, thirty, forty-five, sixty minutes and two hours contact. The tubes of bouillon were incubated for forty-eight hours at body temperature and readings were made. Growth was observed in every tube. The test was repeated using B. typhosus instead of Staphylococcus aureus but performing the test for one hour only. Growth was observed in every tube.

The above tests were repeated but instead of 0.5 cc. of organisms, 0.1 cc. was employed and the temperature of the water bath was 37 degrees C. The test organisms were Staphylococcus aureus, B. typhosus and B. coli (Escherichia coli). Growth was observed in all of the subculture tubes with the exception of the saturated aqueous menthol solution with B. typhosus, in which test growth was observed in all tubes up to thirty minutes and no growth in any tube thereafter.

Since saturated aqueous solutions of menthol and camphor, with the exception of menthol and (0.1 cc. culture of) B. typhosus, did not display any bactericidal action within two hours against the test organisms employed, a series of experiments were carried out to determine whether such solutions exerted any bacteriostatic action.

Saturated solutions in bouillon were prepared by adding several grams of menthol or camphor to 100 cc. of sterile bouillon in 250 cc. flasks. The mixtures were placed in the incubator at body temperature where they were kept for several days, and well shaken from time to time. They were kept at room temperature the night before the test was carried out and the excess of camphor or menthol removed by filtration, under sterile conditions, just before use. One-tenth of a cc. of the test organism was added to each flask (containing the 100 cc. of saturated menthol or camphor in bouillon); the flask was well shaken and dilutions were made and plated immediately to determine the bacterial count. The plates were incubated at 37 degrees C. and counts were made forty-eight hours later. Similar dilutions and platings were made after three hours, six hours, twenty-four hours, seventy-two hours, and one week's contact of organisms and solution. The flasks were kept in the incubator at 37 degrees C. between platings. Control flasks were made also, using 0.1 cc. of the test organism in 100 cc. plain bouillon (as employed in the test), incubating and plating in the same manner as the flasks containing saturated menthol or camphor solutions and organisms. The same three test organisms were employed, namely, B. typhosus, B. coli, and Staphylococcus aureus. These tests were not performed with menthol and B. typhosus as bactericidal action had been displayed by saturated aqueous menthol solutions against B. typhosus (0.1 cc. of culture but not 0.5 cc.) as mentioned above.

The results of these tests are given below:

Saturated menthol in bouillon with Staphylococcus aureus—in most instances no growth after twenty-four hours and in others much less growth than in the control. Bactericidal or bacteriostatic action.

Saturated menthol in bouillon with B. coli—an increase in the bacterial content, but less than the increase in the control. Bacteriostatic action.

Saturated camphor in bouillon with B. typhosus—an increase in the bacterial content which is the same or greater than the increase in the control. No bacteriostatic action.

Saturated camphor in bouillon with Staphylococcus aureus—an increase in the bacterial content which is the same or greater than the increase in the control. No bacteriostatic action.

Saturated camphor in bouillon with B. coli—an increase in the bacterial content, but less than the increase in the control. Bacteriostatic action.

Phenol Coefficient Tests

A solvent of thirty-one parts each of alcohol, glycerin and water and 6.6 grams of soap was used successfully to prepare solutions of menthol and camphor, the following strengths of the latter being employed: 1, 3, 4 and 5 per cent. menthol; 1 and 3 per cent. camphor and a mixture of 1 per cent. menthol and 1 per cent. camphor. The 3 per cent. camphor was the only solution difficult to make as the camphor went into solution only after standing in the incubator at 37 degrees C. over night.

Phenol coefficient tests were performed with all of these solutions and the solvent separately using both B. typhosus and Staphylococcus aureus as the test organisms. The Reddish method, similar to the F. D. A. method, described in Circular 198 of the United States Department of Agriculture (16), was the technique employed in most cases. This test requires a temperature of 37 degrees C. for Staphylococcus aureus and 20 degrees C. for B. typhosus. Such tests were performed and also tests using a temperature of 20 degrees C. for Staphylococcus aureus and 37 degrees C. for B. typhosus, so that results were available using both of these test organisms and both temperatures in each instance.

The Hygienic Laboratory Phenol Coefficient Test, described in Circular 198 (16) was also employed with these different solutions, testing against Staphylococcus aureus at 20 degrees C. and 37 degrees C. and against B. typhosus only at 20 degrees C. The results of all these tests are given in Table 1 and the coefficients calculated both for the solutions and for menthol and camphor are given in Table 2.

A marked increase in the efficiency and phenol coefficients of the solutions will be noted (see tables) against B. typhosus at the temperature of 37 degrees C. (Reddish technique) while a decrease in bactericidal efficiency and phenol coefficients is noted against Staphylococcus aureus at 20 degrees C. as compared with the former temperatures. These experiments bring out strikingly the effects of temperature upon the bactericidal action of these solutions. The

phenol controls also vary depending upon the temperature used. This prevails to such an extent (especially in the case of B. typhosus) that in some instances the increase in bactericidal activity of the solution at 37 degrees C. (as noted by the dilution which kills) is not indicated by its phenol coefficient if, instead of calculating by comparing the solution to be tested at 37 degrees C. with phenol at 20 degrees C., this calculation is made by observing the bactericidal efficiency of phenol dilutions at 37 degrees C. Therefore, in Table 2, phenol coefficients were also calculated for menthol and camphor by comparing the solutions at 37 degrees C. with phenol at 20 degrees C. for both B. typhosus and Staphylococcus aureus. This is a practice employed by some workers and it indicates, to a much greater extent, the increased efficiency of the chemical tested and in this case, menthol and camphor.

It might be of interest to bring again to the attention of workers that it is not proper to regard Gram negative motile rods as B. typhosus just because in the action of such an organism with phenol an identical response as is yielded by B. typhosus and phenol controls in phenol coefficient tests is obtained. Our attention was directed to such an organism obtained from another laboratory and labeled B. typhosus and which, though it yielded identical findings with phenol controls, resulted in different biological findings and in the production of entirely different results with menthol and camphor solutions than those observed in previous tests with a known B. typhosus. It is absolutely essential not only to check the organism as to its behavior against phenol but cultural and biological tests (including the agglutination test) are also necessary safeguards to be certain that one is working with the proper organism.

Summary

(1) Solutions of 1 per cent. menthol, 1 per cent. camphor and a mixture of 1 per cent. menthol and 1 per cent. camphor in liquid petrolatum did not display any bactericidal action in any of the tests performed.

(2) Saturated aqueous solutions of menthol proved bactericidal against B. typhosus within thirty minutes (using 0.1 cc. of culture), and bactericidal against Staphylococcus aureus (0.1 cc. of culture) within twenty-four hours in most instances (bacteriostatic in only one instance); while bacteriostatic action was displayed against B.

coli. Saturated aqueous camphor solutions displayed bacteriostatic action only against B. coli and neither bactericidal nor bacteriostatic action against B. typhosus or Staphylococcus aureus.

(3) Solutions of menthol and camphor in a solvent composed of thirty-one parts each of alcohol, glycerin and water and 6.6 parts of soap, when tested by the phenol coefficient test against B. typhosus and Staphylococcus aureus, yielded the following phenol coefficients for menthol and camphor:

REDDISH TECHNIQUE

Average phenol coefficient of menthol with Staphylococcus aureus—

1.2 at 37 degrees C. compared with phenol at 20 degrees C. (This is the method advocated in computing the findings.)

0.9 at 37 degrees C. compared with phenol at 37 degrees C.

0.4 at 20 degrees C. compared with phenol at 20 degrees C.

Average phenol coefficient of menthol with B. typhosus—

5.6 at 20 degrees C. compared with phenol at 20 degrees C. (This is the method advocated in computing the findings.)

5.3 at 37 degrees C. compared with phenol at 37 degrees C.

10.2 at 37 degrees C. compared with phenol at 20 degrees C.

Average phenol coefficient of camphor with Staphylococcus aureus—

0.5 at 20 degrees C. compared with phenol at 20 degrees C.

No phenol coefficient was calculated for camphor and Staphylococcus aureus at 37 degrees C. because the solutions tested here kill only when undiluted, and the solvent itself also kills when undiluted at 37 degrees C. In the tests with camphor and Staphylococcus aureus at 20 degrees C. the solvent itself does not kill when undiluted, and since the camphor solution does kill when undiluted at 20 degrees C. a phenol coefficient for camphor, under these conditions, can be calculated.

Average phenol coefficient for camphor with B. typhosus—

0.74 at 20 degrees C. compared with phenol at 20 degrees C. (This is the method advocated in computing the findings.)

1.3 at 37 degrees C. compared with phenol at 37 degrees C.

2.5 at 37 degrees C. compared with phenol at 20 degrees C.

HYGIENIC LABORATORY TECHNIQUE

Phenol coefficient of menthol with Staphylococcus aureus—

0.7 at 37 degrees C. compared with phenol at 37 degrees C.

Phenol coefficient of menthol with B. typhosus—

3.0 at 20 degrees C. compared with phenol at 20 degrees C. (This is the method advocated in computing the findings.)

Phenol coefficient of camphor with B. typhosus—

0.98 at 20 degrees C. compared with phenol at 20 degrees C. (This is the method advocated in computing the findings.)

The effect of temperature on the bactericidal efficiency of these menthol and camphor solutions is clearly shown in Table 1, but as the phenol controls also vary with the temperature, in some instances this increase in bactericidal efficiency of menthol and camphor is not indicated by its phenol coefficient at the higher temperature unless the computation is made against the phenol at its standard temperature.

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TABLE 1

Solution	Reddish Technique 0.5 cc. Staph. aureus at 37° C.				Reddish Technique 0.5 cc. Staph. aureus at 20° C.				Reddish Technique 0.5 cc. B. typhosus at 20° C.				Reddish Technique 0.5 cc. B. typhosus at 37° C.				Hygienic Laboratory Technique 0.1 cc. Staph. aureus at 37° C.					Laboratory Technique 0.1 cc. Staph. aureus at 20° C.					Laboratory Technique 0.1 cc. B. typhosus at 20° C.				
	Time	5	10	15		5	10	15		5	10	15		5	10	15		5	7.5	10	12.5	15		5	7.5	10	12.5	15		5	7.5	10	12.5	15
Solvent *	und.	—	—	—	und.	+	+	+	und.	—	—	—	und.	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—
	1–2	+	+	+					1–2	+	+	+	1–2	+	+	+	1–2	+	+	+	+	+	1–2	+	+	+	+	+	1–2	+	+	+	+	+
Solutions in Solvent																																		
1% Menthol	und.	—	—	—	und.	+	+	+	und.	—	—	—	1–2	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—
	1–2	+	+	+					1–2	+	+	+	1–3	+	—	—	1–2	+	+	+	+	+	1–2	+	+	+	+	+	1–2	+	+	+	+	+
													1–4	+	+	+																		
3% Menthol	und.	—	—	—	und.	—	—	—	1–8	+	—	—	1–30	+	—	—	1–2	—	—	—	—	—	und.	—	—	—	—	—	1–5	—	—	—	—	—
	1–2	—	—	—	1–2	+	+	+	1–9	+	+	—	1–35	+	+	+	1–3	+	—	—	—	—	1–2	+	+	+	+	+	1–6	+	—	—	—	—
	1–3	+	+	+													1–4	+	+	+	+	+							1–8	+	+	—	—	—
																													1–11	+	+	—	—	—
																													1–12	+	+	+	—	—
																													1–13	+	+	+	+	+
4% Menthol	1–2	—	—	—	und.	—	—	—	1–25	+	—	—	1–45	—	—	—	Phenol coefficient tests with the Hygienic Laboratory Technique were not performed with the 4 and 5% Menthol solutions.																	
	1–3	+	—	—	1–2	+	+	+	1–30	+	+	+	1–50	+	+	+																		
	1–4	+	+	—																														
	1–5	+	+	+																														
5% Menthol	1–4	+	—	—	und.	—	—	—	1–30	—	—	—	1–60	+	—	—																		
	1–5	+	+	—	1–2	+	+	+	1–35	+	+	+	1–65	+	+	—																		
	1–6	+	+	+																														
1% Camphor	und.	—	—	—	und.	+	+	+	und.	—	—	—	1–2	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—
	1–2	+	+	+					1–2	+	+	+	1–3	+	+	—	1–2	+	+	+	+	+	1–2	+	+	+	+	+	1–2	+	+	+	+	+
													1–4	+	+	+																		
3% Camphor	und.	—	—	—	und.	+	—	—	1–2	—	—	—	1–8	+	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—	1–2	—	—	—	—	—
	1–2	+	+	—	1–2	+	+	+	1–3	+	+	—	1–9	+	+	—	1–2	+	+	+	+	+	1–2	+	+	+	+	+	1–3	+	+	—	—	—
									1–4	+	+	+																			1–4	+	+	+	+	—
																																	1–5	+	+	+	+	+
1% Menthol and 1% Camphor	und.	—	—	—	und.	+	+	+	und.	—	—	—	1–5	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—	und.	—	—	—	—	—
	1–2	+	+	+					1–2	+	+	—	1–6	+	—	—	1–2	+	+	+	+	+	1–2	+	+	+	+	+	1–2	+	—	—	—	—
									1–3	+	+	+	1–7	+	+	—															1–3	+	+	+	+	+
													1–8	+	+	+																		

* und. = undiluted. + = growth. — = no growth.

TABLE 2

Solutions in Solvent	Reddish Technique			Technique		Reddish Technique		Technique			Hygienic		Laboratory Technique		
	0.5 cc. Staph. aureus at 37° C.			0.5 cc. Staph. aureus at 20° C.		0.5 cc. B. typhosus at 20° C.		0.5 cc. B. typhosus at 37° C.			0.1 cc. Staph. aureus at 37° C.		0.1 cc. Staph. aureus at 20° C.	0.1 cc. B. typhosus at 20° C.	
	A	B	C	A	B	A	B	A	B	C	A	B	A	A	B
1% Menthol	0.01	—	—	—		0.01		0.01	1.7	3.3	0.009		0.009	0.009	
3% Menthol	0.02	0.8	1.1	0.01	0.5	0.08	2.9	0.17	5.8	11.1	0.02	0.7	0.009	0.08	3.0
4% Menthol	0.03	0.9	1.2	0.01	0.4	0.27	6.9	0.27	6.9	13.1					
5% Menthol	0.05	1.0	1.3	0.01	0.3	0.36	7.2	0.35	7.0	13.3					
1% Camphor	0.01	—	—	—		0.01		0.01	1.1	2.2	0.009		0.009	0.009	
3% Camphor	0.01	—	—	0.01	0.5	0.02	0.74	0.04	1.5	2.9	0.009		0.009	0.02	0.98
1% Menthol and 1% Camphor	0.01			—		0.01		0.03			0.009		0.009	0.01	

A = Phenol coefficient of the solution.

B = Phenol coefficient of the active princple (menthol or camphor) obtained by comparing the solution with phenol at the temperature of the test.

C = Phenol coefficient of the active principle obtained by comparing the solution with phenol at 20° C.

THE PRODUCTION OF PSEUDOMORPHINE FROM MORPHINE

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PSEUDOMORPHINE may be produced from morphine either by simple oxidation or by catalytic oxidation. Anyone who wishes to study its properties has to make it, as it is not on the market. Its formation also has interest as providing some identification tests for morphine. New methods for its production, and new tests for morphine based on its formation, are given here.

Simple Oxidations

Most of the oxidations of morphine are very difficult to control. Permanganate, for instance, oxidizes morphine first to pseudomorphine in neutral, slightly acid, or slightly alkaline solution, but the pseudomorphine then undergoes oxidation quite readily. Two reliable methods for making pseudomorphine are available in the Basic Ferricyanide method and the Mercury Oxidation method. The former is an old method, but its great worth for producing pseudomorphine almost quantitatively seems to be unrecognized. In addition, some texts give it incorrectly by failing to state that the morphine is treated in alkaline solution. The mercury method was discovered by the writer.

1. Basic Ferricyanide Method.

Dissolve morphine in dilute alkali, or dissolve a morphine salt in water and add NaOH to slight excess. Add potassium ferricyanide solution as long as the ferricyanide is reduced. The yellow ferricyanide changes to practically colorless ferrocyanide, and if the morphine solution was not colored it will serve sufficiently well as its own indicator. When the solution remains yellow on standing for a short time the oxidation is complete.

For best results the alkali should be very little in excess of that combining with the morphine, and the ferricyanide solution should be rather weak. Some $NaHCO_3$ may be used to convert any excess NaOH to Na_2CO_3. A one per cent. solution of $K_3Fe(CN)_6$ is satisfactory. When pseudomorphine is made in quantity the morphine can be weighed, and the required amount of one per cent. ferricyanide calculated and added in portions, with a little additional.

After the oxidation, make the solution acid with HCl, then add NH_4OH in excess, and filter off the precipitated pseudomorphine. Wash the pseudomorphine on the filter twice with water, twice with alcohol, and twice with ether. Prolonged washing is impractical, as it will cause the pseudomorphine to run through the filter, unless perhaps an electrolytic solution is used for washing. If the product is not sufficiently pure it is best to dissolve it in dilute HCl (or in acetic acid) and reprecipitate with ammonia. The recrystallization from ammonia, advised by some texts, is impractical. The product without purification will generally be somewhat contaminated with ferrocyanide. When a very pure product is wanted the method developed by Balls for obtaining pure pseudomorphine hydrochloride can be used.(1)

The equation of the change:

$$2\ \underset{\text{morphine}}{C_{17}H_{19}O_3N} + 2\ K_3Fe(CN)_6 + 2\ KOH \longrightarrow \underset{\text{pseudomorphine}}{C_{34}H_{36}O_6N_2} + 2\ K_4Fe(CN)_6 + H_2O;$$

or more correctly,

$$2\ \underset{\text{sodium morphinate}}{NaOC_{17}H_{18}O_2N} + 2\ Na_3Fe(CN)_6 + 2\ NaOH \longrightarrow \underset{\text{sodium pseudomorphinate}}{(NaO)_2C_{34}H_{34}O_4N_2} + 2\ Na_4Fe(CN)_6 + H_2O,$$

the alkali metals being written as all potassium or all sodium for the sake of simplicity.

It will be observed that the reaction uses up alkali. When the excess of alkali is small and the morphine solution not too dilute, pseudomorphine precipitates during the oxidation process.

The weight of the pseudomorphine after washing and drying, but without further purification, should come to more than ninety per cent. of the theoretical; the product however having a greenish cast and being obviously not entirely pure.

2. Mercury Oxidation Method.

Under certain conditions morphine can be oxidized by means of a mercurous or mercuric salt, with nearly complete conversion to pseudomorphine.

Dissolve free morphine in a small excess of alkali, or add alkali to a solution of a salt of morphine (preferably the hydrochloride)

until the precipitate, if any is formed, is dissolved, and the alkali present in small excess. Add a quantity of mercurous chloride, enough to precipitate the excess alkali as Hg_2O and provide for the oxidation of the morphine. An excess of HgCl does no harm. Heat the mixture to boiling; boil for about one minute, or longer if the quantity of morphine to be converted is large. Cool and add alkali to ensure solution of the pseudomorphine. Then filter, washing out the Hg_2O on the filter with dilute alkali. Add concentrated hydrochloric acid to the filtrate until acid, and if so much pseudomorphine is present that its hydrochloride is precipitated, add water until solution is effected. If the solution does not become perfectly clear with this treatment, filter it again. Then add ammonia to neutralize the acid, and filter off the precipitated pseudomorphine. Wash it with only a little water, then with alcohol, then with ether. If greater purity is necessary, dissolve and reprecipitate, or purify with conversion to the hydrochloride by the Balls method.

Mercuric chloride can be substituted for mercurous chloride, at least with dilute morphine solutions. In concentrated solutions the mercuric salt will form a compound with the morphine, and this interferes with the oxidation.

The equation representing the total change is as follows:

$$\underset{\text{morphine}}{2\ C_{17}H_{19}O_3N} + 2\ HgCl + 2\ NaOH \longrightarrow \underset{\text{pseudomorphine}}{C_{34}H_{36}O_6N_2} + 2\ Hg + 2\ NaCl + 2\ H_2O.$$

This oxidation also uses up alkali.

The yield should be about ninety per cent. of the theoretical, and the product is white.

Other Oxidizing Agents

Most other oxidizing agents, such as iodic acid, bromine, auric chloride, and persulfate in acid solution, yield little or no pseudomorphine under most conditions. The principal product at first formed is usually ortho-diphenol-oxymorphine; that is, the oxidation, as often occurs with phenols, begins with the addition of a second phenolic hydroxyl adjacent to the first.

Catalytic Oxidations

In the catalytic production of pseudomorphine the solution contains (1) morphine, (2) a substance that will oxidize when acted on

by the catalyst, (3) the metallic catalyst, (4) a substance that will hold the catalyst in solution in a complex and make it effective, (5) something to adjust the reaction of the solution to a faint alkalinity, leaving the morphine in solution but causing the precipitation of the pseudomorphine as fast as it is formed, and buffering the solution against its becoming acid.

For (2), hydrogen peroxide, or better, potassium persulfate can be used. As the metallic catalyst, (3), silver has some effect and possibly several metals could be used, but the metal required for a good reaction is copper, pre-eminently the catalytic element. Some metals, be it noted, will cause decomposition of peroxide without oxidizing morphine to pseudomorphine; with a manganous salt, for example, not the morphine but the manganese is oxidized, to MnO_2. The substances of class (4) seem to be all nitrogen compounds, but of different kinds: cyanide, cyanate, pyridine, or nicotine can be used. These compounds confer more or less alkalinity on the solution and thus may serve also for the compound (5). K_2CrO_4, Na_2HPO_4, or $NaHCO_3$ can also be used to adjust the reaction of the solution, or buffer it against its becoming acid when persulfate is used.

The oxidations are:

$$2\ \underset{\text{morphine}}{C_{17}H_{19}O_3N} + H_2O_2 \longrightarrow \underset{\text{pseudomorphine}}{C_{34}H_{36}O_6N_2} + 2\ H_2O,$$

and

$$2\ C_{17}H_{19}O_3N + K_2S_2O_8 \longrightarrow C_{34}H_{36}O_6N_2 + 2\ KHSO_4.$$

(But *direct* oxidation by persulfate produces a different result; catalytic decomposition of dilute persulfate must be used to produce pseudomorphine.)

Only one catalytic method has been published, so far as I know. This is Deniges' method (2), in which a neutral solution of morphine hydrochloride is treated with hydrogen peroxide and potassium cuprous cyanide solution. Although Deniges stated that the yield is only twenty to twenty-five per cent., the method has been used to produce pseudomorphine in quantity. Balls used it (1), prescribing a pH of 6.5 to 6.8; yet he stated that a yield of twenty-five per cent. was a good one. Substituting persulfate for peroxide and pyridine for cyanide results in a much more efficient method.

3. Persulfate—Pyridine Catalytic Method.

Dissolve 1 Gm. morphine hydrochloride in 250 cc. water and add 10 cc. of $CuSO_4$ solution 1:10,000 in copper, 20 cc. of 5% potassium persulfate solution, 15 cc. of 5% $NaHCO_3$ solution, and 5 cc. of pyridine, mixing thoroughly. Pure medicinal pyridine is not necessary as even the "denaturing grade" will have practically the same effect. Let stand 10 minutes, then filter off the precipitated pseudomorphine and wash it with water, alcohol, and ether. Yield about 75%. The product has a yellow color.

Cyanate in place of pyridine will give a good reaction, if the quantities of the other substances are properly adjusted. A much greater concentration of copper is required.

These catalytic reactions are generally sensitive to small amounts of a necessary component, and this one can be used to detect morphine, peroxide, persulfate, copper, cyanide, cyanate, pyridine, nicotine, etc. Of course such a test is non-specific, except for morphine. One example only of such a test, for the detection of pyridine, will be given:

Dissolve a little morphine in 1 cc. of solution to be tested, add 3 drops 1:20,000 copper solution, 4 drops 0.5% potassium persulfate solution, and 2 drops 1% K_2CrO_4 solution. A pyridine solution as dilute as 1:5000 will with this treatment become cloudy within 3 to 4 minutes, and microscopic examination will show crystals of pseudomorphine.

Tests for Morphine by Conversion to Pseudomorphine

It is practically certain that only morphine, together with a few of its closely related and easily decomposable derivatives, such as heroine, will yield pseudomorphine on oxidation. Positive identification of pseudomorphine is therefore equivalent to identification of the morphine from which it was formed, and even a single characteristic test for pseudomorphine is equivalent to a characteristic test for the morphine.

The strong green color yielded by pseudomorphine with Marquis' reagent and an oxidising agent is a highly characteristic test. Also, if formed gradually pseudomorphine will come down in crystalline form and may be recognized by its appearance under the microscope. The former property, with simple oxidation, and the latter, with catalytic oxidation, may be used as tests for morphine without the necessity of

separating the pseudomorphine from the solution in which it is formed.

1. Green Color Test

(a) *Ferricyanide Oxidation*

To ½ cc. of morphine solution add 1 drop of 10% Na_2CO_3 (in excess of that needed to neutralize the solution if it is acid); then add 1% potassium ferricyanide solution drop by drop (if the first drop is decolorized) until the solution is distinctly, though not strongly, yellow. Allow a few moments after the addition of each drop for the reaction. Underlay with 1 to 2 cc. of concentrated sulfuric acid, and add 1 drop of 37-40% formaldehyde solution. Mix while cooling with running water. A bright green color is produced. The test succeeds with a 1:3000 morphine solution; also with fairly concentrated solutions. With a 1:100 (or more concentrated) solution pseudomorphine precipitates during the oxidation. With a 1:50 solution about 20 drops of the ferricyanide are required to color the solution yellow; the test then gives intense dark green.

(b) *Mercury Oxidation*

To about 1 cc. of morphine solution add a drop of 10% NaOH, a large pinch of HgCl, and a drop of 37-40% formaldehyde solution. Heat to boiling and keep near the boiling temperature for a short time, not over a minute. Cool and add 2 to 3 cc. concentrated sulfuric acid; mix while cooling with running water. A bright green color is produced. The HgCl causes a black precipitate, and with dilute morphine solutions it may be necessary to let this settle to observe the green solution. With this precaution the test is easily sensitive to 1:3000. The formaldehyde can be added after the boiling, as it is not concerned in the oxidation of morphine to pseudomorphine. However if it is added after the sulfuric acid has been mixed in and the solution cooled it becomes necessary to add an oxidizing agent to bring out the green color. A few drops of nitric-acid oxidizing solution will do this. (To 50 cc. water add 5 drops concd. HNO_3; mix 1 cc. of this solution with 3 cc. concd. H_2SO_4 for the nitric-acid oxidizing solution.) This variation is a little less sensitive. $HgCl_2$ can be substituted for HgCl. It is perhaps better for dilute solutions as it gives a white precipitate instead of black, but it is unsatisfactory

for solutions of 1:200 or greater concentration because conversion is likely to be incomplete.

2. Crystal Test

(a) *Pyridine*

Treat 1 cc. neutral solution of a morphine salt with 4 drops 0.5% potassium persulfate solution, 3 drops 1:20,000 copper solution, and 2 drops 1:30 pyridine solution. After it has stood a short time examine the solution under the microscope for crystals. Those of pseudomorphine are small plates or leaflets, colorless and transparent, usually square or diamond shaped, but sometimes four-pointed stars. The test is sensitive to a 1:3000 morphine solution and also succeeds with a 1:50 solution. Increasing the pyridine results in a more rapid precipitation, but too much pyridine makes the precipitate amorphous. It is quite possible that a quantitative morphine determination by turbidity measurements could be based on this reaction.

(b) *Cyanate*

With 1 cc. neutral morphine solution use 2 drops 0.5% persulfate, 2 drops 1:2000 copper solution, and 4 drops 1% KCNO solution.

(c) *Cyanide*

Use 3 drops 0.1% persulfate, 3 drops 1:2000 copper solution, and 3 drops 0.5% KCN solution.

(d) *Peroxide With Pyridine*

As an example of the use of H_2O_2: To 1 cc. of a neutral morphine solution add 2 drops of a 1:20 dilution of the ordinary 3% hydrogen peroxide, 3 drops of a 1:10,000 copper solution, and 2 drops of a 1:30 pyridine solution. After the solution has stood a few minutes examine it under the microscope for pseudomorphine crystals.

Summary

1. Pseudomorphine can be manufactured from morphine in alkaline solution with a yield of about ninety per cent. by oxidation with ferricyanide, or by heating with a salt of mercury, as HgCl. It can also be manufactured by catalytic oxidation with a yield of about seventy-five per cent., using persulfate as oxidizing agent, copper as catalyst, and pyridine as the substance with which copper

forms an effective complex. This new catalytic method, and the mercury method, originated with the writer.

2. The production of pseudomorphine can be made a characteristic and fairly simple test for morphine either by utilizing the green color it gives with formaldehyde, sulfuric acid, and an oxidizing agent, or by recognizing its crystals under the microscope. In the color test the morphine is converted by simple oxidation, in the crystal test by catalytic oxidation. These new tests for morphine are sensitive to a 1:3000 morphine solution.

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GLYCOCOLL—Widespread interest has been aroused during the past year among biological chemists and clinicians by the accidental discovery, in connection with researches on metabolism, that glycocoll * greatly improved the condition of certain individuals suffering from progressive muscular dystrophy. This disease, characterized by progressive atrophy of the muscles, had previously been considered incurable and therefore a great therapeutic advance has been made. Not all cases studied have responded to the treatment, but there is evidence for believing that even refractory cases may be helped if the treatment is continued for a sufficiently long time. Subsequent trial of glycocoll in cases of myasthenia gravis indicate that it is possibly of even greater benefit in this condition. Evidence is accumulating that it may find use in the treatment of other diseases primarily involving the muscles.

*Glycocoll, or glycine, is a white, sweet, crystalline amino acid having the formula $CH_2.(NH_2).COOH$. It is given by mouth, dissolved in water, in doses of one-half ounce per day for adults, and two-thirds of this amount for children. It is very slightly soluble in alcohol and insoluble in ether, and is being supplied by the Calco Chemical Company, Eastman Kodak Company, Hoffman, LaRoche Company, and Merck & Co., Inc. Distinction should be made between glycocoll, or glycine, and a toxic proprietary photographic developer marketed as "Glycin."—A. H., Jr.

SKETCH OF THE PROPERTIES OF PSEUDOMORPHINE

By Charles C. Fulton

U. S. Industrial Alcohol Laboratory, Minneapolis, Minn.

PSEUDOMORPHINE is the first oxidation product of morphine. It is formed from two molecules of morphine by the removal of two hydrogen atoms, according to the equation

$$\underset{\text{morphine}}{2\ C_{17}H_{19}O_3N} + O = \underset{\text{pseudomorphine}}{C_{34}H_{36}O_6N_2} + H_2O$$

The oxidation may easily go further.

Pseudomorphine also occurs naturally as a constituent of opium. In fact, it was in this connection that it received the name "pseudomorphine." As an oxidation product of morphine it is often called oxydimorphine or oxymorphine. There are however a number of other alkaloids that are oxidation products of morphine, and hence there are other oxymorphines. The name pseudomorphine is by no means perfectly applicable either, as the resemblance to morphine is not especially close. Several other derivatives of morphine show at least as much resemblance to the parent substance. Pseudomorphine is also called dehydromorphine occasionally.

In opium pseudomorphine occurs to the extent of about .02 to .04 per cent. The alkaloids occurring in greater amount are the six chief alkaloids of opium; namely, morphine, narcotine, codeine, thebaine, narceine, and papaverine; and also, sometimes at least, the minor alkaloids meconidine and cryptopine.

Pseudomorphine is physiologically inert.

Morphine has three oxygen atoms in its molecule; one phenolic, one alcoholic, and one inert. Consequently in two morphine molecules there are four hydroxyl groups, and there is said to be evidence that they all remain intact in the pseudomorphine molecule. At any rate pseudomorphine is a phenol of a kind similar to morphine.

Pseudomorphine is a weak base and very insoluble in water. When precipitated gradually by a slow oxidation of neutral or slightly basic morphine solutions it is crystalline, occurring as small square leaflets, silky needles, or occasionally diamonds or four-pointed stars. It is also crystalline when precipitated from hot acid solution by the addition of ammonia. If formed rapidly, however, or precipitated

suddenly from cold solution, it is amorphous. As the precipitate forms, it has a peculiar "mother of pearl" lustre. This soon disappears. When the precipitate is washed with distilled water or alcohol, though not actually dissolved, it gradually forms a colloidal solution and so passes through the filter. This can be prevented by washing with water containing an electrolyte.

Pseudomorphine is fairly soluble in most acids, but its salts with mineral acids are much less soluble than those of most alkaloids. The sulfate in fact is insoluble in water; a well-marked characteristic, but one sometimes exaggerated, as Balls remarks (1). Concentrated sulfuric acid dissolves it. The alkaloid is readily soluble in acetic acid. It is precipitated by ammonia and is but slightly soluble in excess. However, it is readily dissolved by excess of alkali, due to its phenolic character.

Pseudomorphine is insoluble in the ordinary organic solvents, including alcohol, ether, chloroform and benzene. In this it somewhat resembles morphine, except that morphine is soluble in alcohol.

In precipitation by the alkaloidal reagents pseudomorphine has the general characteristics of other weak insoluble alkaloids of opium, as narcotine, papaverine and apomorphine. It gives crystals with many reagents. Its color reactions are numerous and in general are determined by its phenolic character.

The importance of pseudomorphine in toxicology has been somewhat exaggerated. It is itself easily oxidized, and there seems no adequate proof that it is the usual product of morphine in the human organism. It is known that many oxidations produce no more than traces of pseudomorphine at any time, and it is almost certain that the oxidation of morphine does not necessarily pass through the pseudomorphine stage, though this is contrary to the usual assumption. However, pseudomorphine cannot be ruled out of the subject matter of toxicology, for it is undoubtedly formed in many oxidations.

Toxicologies at present give no identification tests for any oxidation products of morphine other than pseudomorphine.

The writer once found pseudomorphine as the sample submitted in a narcotic drugs case. The whole sample consisted of a number of broken fragments of glass (originally a vial supposed to have contained morphine solution) coated thinly on the concave sides with a white substance, which proved to be pseudomorphine.

Under the proper conditions pseudomorphine can be produced almost quantitatively from morphine. Its formation can be made the basis of laboratory identification tests for morphine. It gives good crystal tests and strong color reactions. It can be used as a reagent for aldehydes. As an alkaloid and as a phenol it is an interesting substance and one well worthy of study.

REFERENCE

(1) Balls: Concerning Pseudomorphine. *Jour. Biol. Chem.*, LXXI, 537.

THE INTERNATIONAL STANDARD FOR THE OESTRUS-PRODUCING HORMONE.—At the request of the officers of the Permanent Commission on Biological Standards of the Health Organization of the League of Nations, the Board of Trustees of the U. S. Pharmacopœial Convention has agreed to assume the responsibility for distributing the International Standard for the Oestrus-Producing Hormone in the United States. Supplies of this material have just been received from the National Institute for Medical Research, London, where the International Standard has been prepared. This Standard is now available for the use of manufacturers of preparations of this Hormone, for the purpose of establishing for their products a uniform potency in the terms of the International Unit; one International Unit consists of 0.0001 mgm. of the Hormone issued by the League of Nations. This material is also available for those carrying out important therapeutic researches in this field.

A memorandum suggesting the course to be followed in using the International Standard, has also been supplied by Dr. H. H. Dale, Director of the National Institute for Medical Research. Those who are interested in securing this memorandum or the International Standard, should communicate directly with E. Fullerton Cook, Chairman of the U. S. P. Committee of Revision, Forty-third Street and Woodland Avenue, Philadelphia, Pa.

THE APOTHECARY, A LITERARY STUDY

By Edward Kremers

No. 43. A Contemporary of Lucca Landuci

IN Schnitzler's drama "Der Schleier der Beatrice" we find depicted a contemporary of Lucca Landucci. He is one Capponi a "Haendler mit Spezereien und Wohlgeruechen" who plied his trade in Bologna during the early part of the sixteenth century. The act in which he plays a role is a street scene toward evening. His stock in trade is contained in small bottles and boxes displayed on two small tables in front of his shop. He himself stands in front of his boutique greeting passers-by. As the curtain rises on the second act, two women approach and the following conversation ensues:

CLAUDIA

Hier ist's.—Guten Abend.

Here it is.—Good evening.

CAPPONI

Guten Abend, meine Damen. Was steht zu diensten?

Good even, my ladies. What can I do for you?

CLAUDIA

Ich moechte ein Flaeschen von Eurem Rosenwasser kaufen.

I should like to purchase a small bottle of your rose water.

CAPPONI

Welche Art von Rosenwasser? Wir haben etwa 25 oder 30 verschiedene. Ach Gott! Das gewoehnliche Paduaver Rosenwasser, das neapolitanische, das zyprische—

What kind of rose water? We have about 25 or 30 varieties. Great God! The ordinary Paduan rose water, the Neapolitan, the Cyprian—

CLAUDIA (impatiently)

Ich weiss nicht wie es heisst, ich hab' es im vergangenen Winter gekauft. Allerdings stand ein ganz anderer da, der es verkaufte, ein huebscher Knabe.

I know not by which name it is called. I bought it last winter. Some one else sold it to me, a handsome lad.

CAPPONI

Bennozzo, my son! Ach Gott!

Bennozzo, my son! Great God!

CLAUDIA

Warum seufzt Ihr? Ist er gestorben?

Why do you sigh? Did he die?

CAPPONI

Was faellt Euch ein! Dass ich seufze, ist eine Angewohnheit, eine ueble Angewohnheit, wenn Ihr wollt, oder auch eine philosophische Angewohnheit. Aber um auf das Rosenwasser zurueckzukommen, so koennte es immerhin auch das persische gewesen sein.

What do you think! That I sigh is a matter of habit. As you look at it, it may be a bad habit, or possibly a philosophical habit. However, to come back to the rose water, it may have been the Persian.

CLAUDIA

Ja, so nannte es Euer Sohn.

Yes, that is the name by which your son called it.

CAPPONI

Gleich wird es zu Euerer Verfuegung sein, werte Frau! Ich hab' es dahinten aufbewahrt. Stuend' es hier vorn mit den andern, so haett' ich den ganzen Tag alle junge Maedchen und Frauen von Bologna vor dem Laden stehen und die jungen Leute natuerlich dazu. Ach Gott! Und ein jeder moegte sich eine Nase voll nach Hause bringen, ohne dafuer zu zahlen.

You shall have it immediately, dear madam. I keep it in the rear. If it stood here with the others, all the young girls and women of Bologna would stand here all day long, And the young men, naturally, also. *Mon dieu,* every one would like to take a nose full home without paying for it.

CLAUDIA (to Caterina)

Ninm doch auch ein Flaeschchen!

Why do you not also take a small bottle?

CATERINA

Wozu? Ich brauche nichts dergleichen. Ich thue nichts anderes, als jeden Morgen den Saft einer sizilianische Orange in mein Bad traeufeln lassen, das genuegt vollkommen.

Why should I? I have no use for anything of the sort. All I do is to express the juice of a Sicilian orange into my bath every morning. That is sufficient.

CLAUDIA

Mein Mann liebt es, wenn meine Haut nach Blueten duftet, nicht nach Fruechten.

My husband prefers to have my skin fragrant with the perfume of flowers, not that of fruits.

CAPPONI (reappearing and offering the bottle to the customer)

CLAUDIA

Ja, das ist sie! Rieche doch daran, Caterina! Nun was sagst du?

Yes, that is the one. Smell of it Caterina. What say you?

CATERINA

Nun ja, wenn ein Mann nicht mehr ganz jung ist—

Well, if a man is no longer very young—

CLAUDIA

Da habt Ihr Euer Geld.

Here you have your money.

CAPPONI

Um Vergebung, schoenste Frau! Ihr gebt mir gerade den zehnten Teil von dem, was ich zu bekommen habe!

Pardon, most beautiful of women. You offer me just one-tenth of the sum due me.

CLAUDIA

Ich weiss doch, was ich im Winter dafuer bezahlte.

Well, I know what I paid for it last winter.

CAPPONI

Ja, das waren andere Zeiten! In ein paar Tagen wird man mir das Hundertfache fuer diese Flasche bezahlen. Alles wird teurer. Es giebt keine Moeglichkeit mehr, die Waren in die Stadt zu bringen! Alle Verbindungen sind abgeschnitten! In acht Tagen haben wir die Hungernot, wenn wir ueberhaupt noch am Leben sind, was mir hoechst zweifelhaft ist —womit ich die Damen aber nicht beleidigen will.

Yes, those were other times! In a few days one will pay a hundred times as much for this vial. Everything is going to be more expensive. It is impossible to bring goods into the city any longer. All connections are cut off. In eight days there will be a famine, provided we are still alive, which is very doubtful. But I have no desire to insult the ladies.

CLAUDIA

Dann giebt man Euch keinen Groschen mehr fuer Euer Rosenwasser. Nun sagt mir aber ehrlich: was ist darin enthalten? Es kann nicht nur der Saft von Rosenblaettern sein.

If that be the case, they will no longer give you a farthing for your rose water. But now, tell me truly: what is contained therein? It cannot be only the juice of the rose petals.

CAPPONI

Was sollte es anders sein?

What else should it be?

CLAUDIA

Ist es nicht irgend etwas, was man sonst Liebestraenken beizumischen pflegt? Ich habe Gruende es anzunehmen.

Is it not something which is commonly added to love potions? I have reasons to assume this.

CAPPONI

Was faellt Euch ein! Ich heisse Capponi, wohlgemerkt: Capponi! Und gebe ich mich nicht mit den sonderbaren Mischungen ab, wie andere Leute, wie Basini zum Beispiel!

What do you suppose! My name is Capponi. Please note: Capponi. I have nothing to do with such queer mixtures such as other people sell, Basini for example.

CATERINA

Was gibt's bei Basini?

What can you get at Basini's?

CAPPONI

Gott behuete mich, davon zu reden. Ich koennte ihn an den Galgen bringen und die Damen, die bei ihm kaufen, nicht minder! Ach Gott!

God forbid that I should say anything about it. I might send him to the gallows and no less the ladies who buy from him. *Mon dieu!*

CATERINA

Was sagt Ihr? (Zu Claudia.) Gestern erst habe ich deine Schwester in seinen Laden treten sehen.

What did you say? (Turning to Claudia.) Only yesterday I saw your sister step into his shop.

CAPPONI

Er koennte zwar sagen, es ist Zufall, dass man ihn nachts in der Naehe des Friedhofs umherstreichen sieht; aber ist auch das Zufall, dass er neben der Friedhofsmauer um Mitternacht mit den Naegeln die Erde aufkratzt? Nun, ich will nicht mehr sagen, um so mehr, als Basini nichts anderes tun kann, wenn er sich seine Kunden erhalten will. Denn bei ihm kaufen nur Frauenzimmer, die Ungeheuerlichkeiten noethig haben, um ihre Liebhaber zu entflammen; zu Eurem ergebenen Diener hingegen kommen die schoensten Frauen von Bologna, die nur zu laecheln brauchen, um aus jedem Mann zu machen, was sie wollen!

True, he might say that it was but accidental when he was seen strolling in the neighborhood of the cemetery at night. But is it mere accident when he digs with his fingernails into the earth next to the churchyard wall at midnight? Well, I shall say nothing further, all the more since Basini cannot do otherwise if he wants to retain his customers. For those who purchase at his store are but women who are in need of dreadful means to inflame their lovers. To your obedient servant, however, come only the most beautiful women of Bologna. All they have to do is to smile to make any man do what they want of him.

BASINI

(ist langsam die Strasse von rueckwaerts nach vorne gekommen. Es ist ein langer, hagerer, aeltlicher Mann, der die anderen mit Ueberlegenheit behandelt.)

Guten Abend!

(has come down the street from the rear. He is a long, spare, elderly man, who regards the others with an air of superiority.)

Good evening.

CAPPONI

Das ist er. (Er macht den Frauen Zeichen.) Eben hab' ich von deinen vorzueglichen Gewuerzen und Seifen gesprochen, mein teurer Basini.

There he is. (Motions to the women.) I have just spoken of your precious spices and soaps, my dear Basini.

BASINI

Hat er gesagt, dass ich ein Giftmischer bin?

Did he say that I am a poison monger?

CATERINA

So was Aehnliches!

Something of the sort.

BASINI

Tut nichts, morgen sind ja doch alle Menschen gleich in Bologna, Giftmischer wie ich und Ehrenmaenner wie du!

It makes no difference. Tomorrow all people of Bologna will be alike, poison mongers such as I and men of honor such as you.

CAPPONI

He, Basini, bist du so verzagt? Ich nicht! Unsere Mauern sind stark, und unser Herzog ist ein Held!

Ho there, Basini, are you so discouraged? Not I. Our city walls are strong and our duke is a hero.

BASINI

Was hilft das alles gegen einen Teufel wie Borgia?

What good will all of this do us against such a devil as Borgia?

CATERINA

Teufel, sagt Ihr? Er soll so schoen sein!

Devil say you? He is reported to be so handsome.

CAPPONI

Der Borgia ist noch weit—hehe!

Borgia is still far away—haha!

BASINI

Nicht so weit, als Ihr glaubt. Wie waer' es sonst zu erklaeren, dass man hier weiss, was er geschworen hat?

Not as far as you imagine. How else could you explain that we know here what oath he has sworn yesterday?

CAPPONI

Nun, was hat er geschworen?

Well, what sort of oath did he utter?

BASINI

Dass er ein fuerchterliches Gericht ueber diese gottlose Stadt halten wird.

That he will pass a fearful judgment upon this Godless city.

CAPPONI

(erschrickt zuerst; dann schlaegt er Basini auf die Schulter.)
Immer erzaehlt er Schnurren! (Zu den Frauen.) So ist er—hab' ich's nicht gesagt?

(is frightened at first. Then he slaps Basini on the shoulder.)
You always like to relate jokes. (To the women.) Such is he—did I not tell you?

BASINI

Nun, was mich anbelangt, ich habe meinen Laden gesperrt und tu' ihn nie wieder auf.

(Soldaten ziehen vorbei.)

Well, so far as I am concerned, I have closed my shop and never shall I open it again.

(Soldiers march by.)

But for his habit of sighing and his stilted language, this Bologna apothecary of the early years of the sixteenth century might be taken for a modern salesman with as much conscience as the average radio advertiser of today. Neither does lack of cooperation appear to be a modern characteristic of the commercialized druggist. His insinuating remarks about his competitor would appear to be ample proof of this statement.

If recent investigators of drug store stock have pointed out the excessive overhead due to the large number of commercial varieties of cosmetics, this condition also does not appear to be new, for Schnitzler's salesman of perfumes boasts of from twenty-five to thirty kinds of rose water. He enumerates two Italian makes, viz., the Paduan and the Neapolitan, also the Cyprian, but concludes by saying that the Persian is the best, presumably because it is supposed to be the original rose water, just as the "Maria Farina, gegenueber dem Juelichsplatz" was advertised as the best Eau de Cologne because it claimed to be the original commercial article.

Neither do war inflation prices appear to be anything new. In anticipation of the siege he has already raised the price threefold. When the fair customer objects, he claims that in a few days prospective customers will pay a hundredfold. The wily purchaser, however, is his equal and insists that, if his statement comes true, no one will give him anything for his toilet articles.

Whether Schnitzler made a thorough study of the Italian apothecary of the early decades of the sixteenth century may well be doubted. The commercial peculiarities which he describes are not characteristic of Italian representatives, nor of any age. More typical of the age is possibly the allusion to the love potion and the assumed legal restrictions placed upon its traffic.

REPRINTED ARTICLE

AGAR-AGAR AND PARAFFIN EMULSIONS*

*Reprinted from *The Pharmaceutical Journal*, Sept., 1933.

Extemporaneous Preparation

By C. L. M. Brown, Ph. C., and E. A. Lum, Ph. C.

THERE is a very evident need at the present time for a suitable formula for the extemporaneous preparation of an emulsion of agar-agar and liquid paraffin, and this fact is strongly supported by the number of machine-made agar-paraffin emulsions now on the market and by the absence of a formula in the B. P. C.

The formulæ given by Martindale in the "Extra Pharmacopœia" (nineteenth edition, Vol. I, p. 658) and by Elsenbury (P. J., 1932, 74, 315) were tried out, but were not found entirely satisfactory.

In order to find the maximum amount of agar-agar that could be used for emulsification without any separating out, a number of emulsions were made containing various percentages. The results are summarized in Table I:

Per cent. of Liq. Paraffin	Agar 2.0 per cent.	Agar 1.5 per cent.	Agar 1.0 per cent.	Agar 0.6 per cent.	Agar 0.3 per cent.	Agar 0.1 per cent.
30	Coarse Emulsion Agar separates	Coarse Emulsion Agar separates	Coarse Emulsion Agar separates	Coarse Emulsion Agar separates	Coarser Emulsion No separation of Agar	Very coarse Emulsion No separation of Agar
50	Coarse Emulsion Agar separates	Coarse Emulsion Agar separates	Coarse Emulsion Agar separates	Coarse Emulsion No separation of Agar	Coarser Emulsion No separation of Agar	Very coarse Emulsion No separation of Agar

It was evident at this stage that the maximum of agar-agar that could be used was below 1 per cent.; that a "fine" emulsion could not be made by hand using agar-agar alone, and also that a maximum of agar-agar could only be kept in solution *by careful manipulation.* The addition of a number of other emulsifying agents was therefore tried. In every case 50 per cent. paraffin and 0.67 per cent. agar-agar was used. The results are shown in Table II:

Substance	Per cent.	Type	Appearance	Keeping Properties
Gelatin [1]	0.7	W/O	Too coarse Gelatin separates	Decomposition in 5 days
Gelatin [1]	0.2	W/O	Too Coarse No separation	Decomposition in 5 days
Albumen [1]	2	O/W	Too coarse	Decomposition in 24 hours
Casein [1]	4	O/W	A "fine" emulsion A little agar separated	Decomposition in 2 days
Pot. oleate	1.5	W/O	Coarse emulsion Separated 24 hours	Stable
Acacia	3	O/W	A "fine" emulsion but with a tendency to separate	Stable
Acacia	2	O/W	Ditto	Stable
Acacia	1	O/W	A "fine" emulsion Definite separation	Stable
Tragacanth	3	O/W	Rather coarse emulsion Did not separate	Stable
Tragacanth	2	O/W	Ditto	Stable
Tragacanth	1	O/W	Coarse emulsion Tendency to separate	Stable
Acacia Tragacanth	3 1	O/W	A "fine" emulsion but paraffin globules visible. Separation commenced at end of 16 days	Stable

[1] With chloroform, 1-1000.

It is interesting to note that although agar-agar and potassium oleate independently produce o/w emulsions, together they produce a w/o emulsion. The best emulsion was obtained by a combination of agar-agar, acacia, and tragacanth, and the following formula was therefore built up:

Agar-agar	17½ grains
Sodium bicarbonate	10 grains
Powdered acacia	60 grains
Powdered tragacanth	20 grains
Glycerin	6 drachms
Liquid paraffin	3 ounces
Water	to 6 ounces

Triturate the sodium bicarbonate, tragacanth, and acacia to a smooth paste with the glycerin. Dissolve the agar-agar in two fluid ounces of boiling water, and, whilst still boiling, add to the contents of the mortar, stirring briskly. Triturate for about one minute, then add the liquid paraffin two or three drachms at a time, triturating well after each addition. Continue trituration till cold. Stand for an hour (or longer) and again triturate for about five minutes. Transfer to a measure and make up to volume with water.

Our experience indicates that to prepare the emulsion without agar-agar separating is a matter of technique, and requires a little practice. We should like to bring to the notice of readers a comparatively cheap hand-worked emulsifying apparatus, which will be found useful for preparing all types of emulsions. [A descriptive note on this piece of apparatus and illustration was given in *The Journal,* September 2, p. 315.—EDITOR.]

The following formula gives a good emulsion with this apparatus, and is easily twice as "thick" as the one prepared by hand:

Agar-agar	15 grains
Sodium bicarbonate	6 grains
Liquid paraffin	3 ounces
Powdered tragacanth	5 grains
Powdered acacia	5 grains
Glycerin	2 drachms
Water	to 6 ounces

One of us (C. L. M. Brown) would like to express his thanks to the directors of Blackwell, Hayes and Co., Ltd., Birmingham, in whose laboratory part of this work was carried out.

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Elsenburg, J.: *Pharm. Weekblad,* Vol. 69, 300, through *The Pharmaceutical Journal,* 1932, 74, 315.

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MEDICAL AND PHARMACEUTICAL NOTES

THE BRITISH GO ML!—The Chemical Divisional Council of the British Standards Institution* has decided that in all their standard specifications the unit of volume shall be the millilitre (abbreviation ml). This step should stimulate the universal acceptance of the millilitre as the unit of volume, and thus do away with a lot of confusion consequent upon the inaccurate use of the term "c.c."

A short résumé of the history of the metric units of volume will provide the argument in support of the decision. The volume of a cube each side of which is of unit length becomes automatically the unit of volume. If the length of each side were one centimetre, the cube becomes one cubic centimetre, and this is the true interpretation of that volume. Although it is easy to obtain accurately the linear dimensions of a body of simple geometric shape, it is extremely difficult to determine the capacity of a hollow vessel, to be used in measuring liquids, from measurements of its internal dimensions. On the other hand, it is quite easy to obtain the weight of a liquid (say, water) required to fill the vessel. Hence units of volume came into being which were not defined in terms of unit of length, but as volumes occupied by specified weights of a particular liquid—usually water. The founders of the metric system hoped to unify these two systems by defining the kilogram as the mass of a quantity of water which at its temperature of maximum density occupied one cubic decimetre, and to this end Lavoisier and Hauy made a provisional standard kilogram and Lefevre-Gineau and Fabbroni were entrusted with the construction of the standard afterwards known as the "Kilogram des Archives."

THE KILOGRAM DES ARCHIVES

Although this work was carried out with great care and skill, serious doubts arose, during the nineteenth century, as to whether the Kilogram des Archives did represent accurately the definition of the kilogram. The results of numerous investigations proved that there was a small error in this standard kilogram. However, it was

*Report on Metric Units of Volume, British Standards Institution, No. 501—1933. Price 2s.

decided to abandon the original definition of the kilogram and accept the Kilogram des Archives as the actual standard. Thus the kilogram is not the weight of a cubic decimetre of water at its temperature of maximum density, but simply the mass of the cylinder of platinum-iridium alloy known as the International Prototype Kilogram. In 1901 the litre was defined as the "volume occupied at its temperature of maximum density, and under normal atmospheric pressure by a quantity of pure water having a mass of one kilogram." This volume is therefore absolutely independent of the metric units of length, and therefore differs from 1000 cubic centimetres, which is simply the volume of a cube of those dimensions, and is not connected with the volume of a certain mass of water.

As a result of numerous determinations the relationship existing between these two units was found to be:

1 litre = 1000.028 cubic centimetres.

Although the difference between one cubic centimetre and one millilitre as shown above is so small as to be negligible, further confusion has arisen due to the misuse of the term cubic centimetre. Few students escape being told that a cubic centimetre is the volume occupied by a quantity of water which weighs one gram. This would be true only if the Kilogram des Archives had been made with absolute accuracy, and the weighing of the water were done at 4 degrees C. and *in vacuo*—conditions which are clearly impracticable. Actually a quantity of water which at 15 degrees C. has an apparent weight in air of one kilogram has, at that temperature, a volume of nearly 1002 cubic centimetres. If glassware were graduated under these conditions the error would be serious. Fortunately British manufacturers of volumetric glassware for a number of years have calibrated their apparatus in terms of the millilitre, and hence when we speak of the "c.c." in most cases we mean the millilitre. The term "c.c." is hard to kill, and even in pharmacy it is still used, although the B. P. 1914 adopted the millilitre. For these reasons the report of the British Standards Institution should be welcomed, as, by virtue of its authority, it will help to lead us in the right direction—to call a spade a spade, or in other words to call a millilitre a millilitre and not a cubic centimetre.—(The *Pharm. Jour.*, Sept., 1933, p. 522.)

EDITOR'S NOTE: The British did not err as we did when we abbreviated the milliliter (U. S. P. IX) to *mil.*, and when, by the same foolish system, our milligram would have been a *mig.* and our millimeter a silly *mim.* Additionally it must be remembered that the abbreviation *mil.* has long been established in metrologic nomenclature as representing the thousandth of an inch.

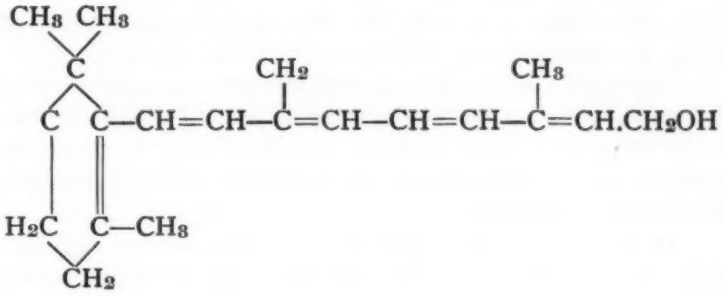
THE VITAMINS—(UP-TO-DATE)

Name	Occurrence	Properties	Effect of Cooking	Effect of Deficiency on Human Body
A	Halibut liver oil, cod liver oil, mammalian liver oils, milk, butter, eggs, leafy vegetables and salads, carrots, some fruits (orange)	Soluble in fat-solvents, easily oxidised, heat stable in absence of air	Destruction dependent on chances of oxidation	Cessation of growth when body reserves are exhausted Keratinisation of epithelium of eyelids, respiratory tract, vagina, etc.
B_1	Dried yeast, embryos of seeds, most leafy vegetables, organs and muscles of many animals, milk (little)	Soluble in water, heat labile especially in alkaline solution	Easily destroyed	Cessation of growth Development of beri-beri.
B_2	Dried yeast, milk, egg-white, most leafy vegetables, organs and muscles of many animals	Soluble in water, more stable to heat than B_1, but not entirely so	Less easily destroyed than B_1	Cessation of growth Development of pellagra (probably)
B_3	Wheat, air-dried yeast	Soluble in water, thermolabile	Easily destroyed	So far only shown to be necessary for the pigeon's maintenance of weight
B_4	Yeast	Soluble in water, thermolabile	Easily destroyed	So far only shown to be necessary for the rat which, without it, develops muscular weakness, spastic gait, humped back, etc.
B_5	Yeast, whole wheat	Soluble in water, stable to heat and alkali	Not destroyed	So far only shown to be necessary for the pigeon's maintenance of weight
Y (possibly allied with the B vitamins)	Yeast	Soluble in water, stable to heat and alkali	Not destroyed	So far only shown to be necessary for growth of the rat
C	Practically all fresh fruit and vegetables, germinated peas and beans	Soluble in water, easily oxidised though fairly stable at pH 2.2 (the acidity of lemon juice)	Very easily destroyed	Development of scurvy Changes in the dentine of teeth
D	Cod-liver oil and some other fish-liver oils, butter and milk (little)	Soluble in fat-solvents, more stable than vitamin A though not completely so	Slight destruction	Retardation of growth Development of rickets Unsound formation of teeth
E	Wheat-germ, green vegetables and salads	Soluble in fat-solvents, heat stable, not oxidised by exposure to air	Not destroyed	So far only shown to be necessary for rats and mice and possibly hens Retardation of growth Degeneration of seminal vesicles in males Resorption of Fœtuses in females

(Compiled by Katharine H. Coward, D. Sc., *Pharm. Jour.*)

Constitution of the Vitamins

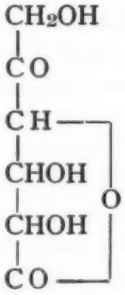
VITAMIN A.—Nearly pure, if not quite pure, preparations have been made. The formula probably is $C_{20}H_{29}OH$, and the suggested structural formula is:—



VITAMIN B_1.—The most active material yet obtained is a colorless crystalline solid of the formula $C_{12}H_{17}O_2N_4S.2HCl$ or $C_{12}H_{20}O_2N_4S.2HCl$.

VITAMIN B_4.—The most active material yet obtained free from other parts of the B complex is a colorless crystalline solid of the formula $C_4H_4N_4.HCl.\frac{1}{2}H_2O$.

VITAMIN C is almost certainly a hexuronic acid named ascorbic acid, $C_6H_8O_6$. The suggested structural formula is:—



VITAMIN D.—Calciferol is almost certainly the pure vitamin, $C_{27}H_{42}O$.

No formulæ have yet been proposed for the other vitamins.—(*Phar. Jour.*)

LEFT-HANDED—LEFT-EARED, LEFT-EYED TOO—According to Dr. George Kreezer, of the Vineland Training School, in a research conducted at Berlin, there is a certain consistency in errors of perception.

If you see a light of a certain intensity, and again, a few seconds later, see a light of exactly the same intensity, you will probably judge the second light to be brighter than the first.

If you see a light a little to your left and then another of exactly the same intensity a little to your right, you will judge the left light to be brighter. Some persons—and they may be those with a tendency to left-handedness—are exceptions and consistently judge the right to be brighter.

If you hear a tone at your left and then another of exactly the same intensity at your right, you will judge the right tone to be louder—you will, that is, if your are one who judged the left light to be brighter. If you are one who sees the right light as brighter, you will hear the left tone as louder.

Thus errors of hearing are consistent with—although opposite to—errors of vision. Yet each type of signal comes to the brain through separate sense organs and over separate networks of the brain's telegraph wires, the nerves.

These perception errors are not due to differences in the sense organs. Neither are they a matter of the nervous pathways to your brain. That has been established. They depend upon the brain itself. They indicate that a certain organization must exist in the brain which in some respects at least conforms to the space-time organization of the material world outside the self, and helps us to account for our perception of that world.

"THE PLAY'S THE THING"—Among the many things that have come through the doors of the drug store back room have been opera singers, musicians, movie and radio stars, scientists, prize fighters, financiers, actors, all sorts and conditions of men. It has been the stepping stone to fame and, on rare occasions, to fortune.

The older generation of pharmacists tell delightful stories of the drug store back room as the meeting place for clerks, in which there were sessions of orchestras, debating societies, where literature, art and baseball were discussed, and where dramatics were fostered.

The histrionic art gained one of its most famous exponents when John Edmond Owens, a clerk in the drug store of Samuel Johnson, of Tenth and Buttonwood Streets, Philadelphia, became an

actor. Owens was evidently stagestruck from his early youth, and his fellow clerk, James Woodhouse, had a like longing.

One day, when customers were few and the boss was away, these two were practicing the fifth act of "Hamlet" in the back room of the store. Woodhouse was Laertes, and Owens, wrapped with a tablecloth for a cloak, was Hamlet. In the grand climax, Owens threw aside his "inky cloak" and exclaimed: "This is I, Hamlet the Dane!" There was a grand crash of glassware, as bottles and graduates from nearby shelving were swept to the floor. What a fall that was!

While still a drug clerk, Owens obtained a position as "supe" under William E. Burton, the then great comedian, "hooking it" from the store and from his parents. His first real part was in the National Theatre, of Philadelphia, as a member of the cast of "The Ocean Child." Here he played the part of Peter Poultice (an apothecary's apprentice). From this on his course before the footlights was onward and upward. He attained most marked success as an actor, playwright and manager.

He made the character of "Unit," in a rather dull dramatic comedy, a star part, and he also made a success of the character of Caleb Plummer.

In his day Owens became the greatest American comedian. His most popular work was the creation of "Solon Shingle." In this character he portrayed a simple-minded, shrewd New England farmer whose greatest earthly possession was "a barrel of apple sass in the tail end of my wagon." Owens made of this driveling old farmer a perfect and lovable specimen of his species. When Owens died he took Solon Shingle with him.

Some of the natural characteristics of Owens stood him well as a drug clerk, and in the buskin he had a most affable manner. He was overflowing with good nature and sympathetic kindness, which won the heart of every person with whom he came in contact. He carried his audience with him and they learned to love and to sympathize with him and with the character which he portrayed.

Owens had a memory which enabled him to remember the name, character and dosage of every drug in the store. He could recite the number and ingredients of prescriptions for months after putting them up.

With his talent and industry he would probably have achieved success as a pharmacist. Through his art he gained position, fortune and deserved admiration.—(F. B. Kilmer.)

PANTOTHENIC ACID—*Science Service* reports that all life may involve the presence of a powerful growth-stimulating acid which has been found in many different kinds of plants and animals and has been concentrated by Dr. Roger J. Williams and Carl M. Lyman, of Oregon State College, to a potency one thousand times stronger than any previously reached.

Because of the widespread occurrence of this little-known substance Dr. Williams, who reported his latest researches to the American Chemical Society, has tentatively named it "pantothenic" acid from the Greek for "from everywhere." The name is justified by tests which show that pantothenic acid was obtained from all sources examined so far which include: cattle, human and chicken liver, milk, crab eggs, sea urchin eggs, planarian worms, earthworms, oysters, bacteria, molds, yeast, mushrooms, potatoes, apples, grains, algae and soil.

"It is probably safe to say that this acid is more widely distributed in nature than any other physiologically potent substance," Dr. Williams declared. "The evidence shows that it is contained in all living substances from the highest mammalian form down to the lowliest worm and from the highly developed green plant down to the tiniest yeast, mold or bacteria.

"The acid was discovered because of its effect on yeast growth," he continued. "When placed in a solution in which yeast is growing it may increase the rate of multiplication from ten to twenty thousand fold in eighteen hours. The fact that it is apparently present in all living cells suggests that it may act as a growth regulator in all cells. It is interesting to observe that yeast and mushrooms, which proverbially grow rapidly, are comparatively very rich sources of the acid."

As recently concentrated by Dr. Williams and his associate, pantothenic acid is so potent in speeding up the growth of yeast that a quantity much smaller than the head of a pin has a detectable effect when placed in 250 gallons of solution in which yeast is growing. The presence of one part of the preparation in one billion parts of yeast culture medium is noticed by the resulting growth increase.

"While the origin of this acid in nature is obscure, except for the fact that it is produced by certain molds in soils, for example," Dr. Williams explained, "we are led to suspect that it is one of the unidentified water-soluble vitamins. In fact, several of its properties at first suggested a close relationship to vitamin G; yet unlike the widely known vitamins it appears to be a substance that even plants cannot make for themselves, but must obtain directly from the soil."

BOOK REVIEW

How Plants Get Their Names. L. H. Bailey. The Macmillan Company, Publishers. $2.25.

Mr. Bailey's recently published volume, "How Plants Get Their Names," combines a history of plant nomenclature and two extensive lists of generic and specific names likely to be met in horticultural literature. As the book is narrative rather than technical in style its usefulness and appeal will not be confined to the experienced botanist, but will attract and instruct all lovers of gardens as well as pharmacists who daily handle the products of the plants noted in the book.

In the first chapter Mr. Bailey points out various errors in naming plants and explains, with considerable detail, the sources of these errors. The Jerusalem Cherry, for instance, is not a cherry and does not come from Jerusalem. Its true name is Solanum Pseudo-Capsicum, and it is closely related to all other Solanums, including true bittersweet, eggplant, and potato, of the nightshade family.

One may also learn from these first pages that geographical names are frequently applied to plants which are native to far-distant places. The garden flower, so-called African marigold, really originated in Mexico. The Cherokee rose, naturalized in our Southern States, is from China. Neither California privet nor California pepper tree are natives of California. Bethlehem sage is not Judean, and Spanish cedar is neither a cedar nor a conifer, and its true habitat is the West Indies.

This will remind the druggist that his Mexican scammony probably is not always obtained from a plant originating in Mexico, that his Chinese rhubarb may not have any connection with China, and that his Jamaica ginger did not come from a plant native to the famous Carribean island.

After brief mention of the early botanists, Gronovius, Royen, Johann Bauhin, Carolus Clusius, Ray and Tournefort, Mr. Bailey devotes considerable space to a comprehensive account of the achievements of Carl Linnaeus, whose outstanding contribution to biological science was in the systematic classification and nomenclature of plants.

It has been tritely stated—"Plants were named by Adam; Linnaeus put them into groups." It is undoubtedly a historical fact that a crude primitive system of plant classification and nomenclature

which antedates all botanical writing did exist. It is also a historical fact that plant genera did not obtain a fair recognition until Tournefort; nor species as distinguished from varieties until Linnaeus; nor families before Addison.

From Linnaeus and his inauguration of the binomial system the author of this book leads on to the subject of the identification of plants, which is of particular interest to all botanists and to plain dirt gardeners, as well as to pharmacists.

The lists of generic and specific names which Mr. Bailey has compiled will be exceedingly useful to those who possess the book because they are marked to indicate the pronunciation and contain, in addition, suggestions for botanical application.

With the aid of this book, the gardener, the florist and the man who handles drug plants and their products can all "speak the language."

F. B. KILMER, Ph. M., New Brunswick, N. J.

October 5, 1933.

LIFE'S GREATEST CHEMICAL—CHLOROPHYLL.—The hemin or red coloring matter of blood is closely related to chlorophyll, and was probably derived from it ages ago. It has iron in place of the magnesium of the chlorophyll. Willstätter recently stated the principal characteristic of animal chemistry as oxidation, catalyzed by the iron of the blood hemin, and of plant chemistry as reduction, catalyzed by the magnesium of the chlorophyll. With the aid of the chlorophyll granules in plants, employing the energy of sunlight, carbon dioxide is converted into sugar, and from that into starch and cellulose: food, reserve food, and structural materials, respectively. Animals ultimately subsist on plants, which in turn utilize the services of chlorophyll. It may not be too much to call chlorophyll the most important organic chemical, for it has made possible life, as we know it, on this earth.—(*A. D. L. Bulletin.*)